Review Article

Cardiovascular magnetic resonance in Tetralogy of Fallot—state of the art

Anna Nyström[1,2], Caroline Berntsson[2,3], Zacharias Mandalenakis[4,5], Kerstin Lagerstrand[2,6], Frida Dangardt[5,7]^, Charlotte de Lange[1,2]^

[1]Department of Pediatric Radiology, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden; [2]Institute of Clinical Science, Sahlgenska Academy, University of Gothenburg, Gothenburg, Sweden; [3]Department of Thoracic Radiology, Sahlgrenska University Hospital, Gothenburg, Sweden; [4]Adult Congenital Heart Unit, Department of Internal Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden; [5]Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [6]Department of Medical Physics and Biomedical Engineering, Sahlgrenska University Hospital, Gothenburg, Sweden; [7]Children's Heart Centre, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Region Västra Götaland, Gothenburg, Sweden

Contributions: (I) Conception and design: C de Lange, A Nyström; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Charlotte de Lange, MD. Associate Professor, Department of Pediatric Radiology, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Behandlingsvägen, 7, S- 416 15 Gothenburg, Sweden; Institute of Clinical Science, Sahlgenska Academy, University of Gothenburg, Box 426, S- 405 30 Gothenburg, Sweden. Email: charlotte.de.lange@vgregion.se; charlotte.de.lange@gu.se.

Abstract: Tetralogy of Fallot (TOF) is the most common type of cyanotic congenital heart disease expressing different severity. There is an increasing survival into adulthood and most patients now experience a good quality of life. Still, complications will develop over time related to the primary surgery and the resulting remodeling of the heart and vessels, which will require reintervention or operation several times during their lives. Imaging plays an increasingly important role in the diagnosis and follow-up of these patients, such as echocardiography as the basic modality, as well as computed tomography angiography (CTA) and cardiac catheterization, providing important anatomical data and the possibility for interventional treatment. Cardiovascular magnetic resonance (CMR) imaging is increasingly used and has a central role in finding the optimal time point for reintervention and provides excellent morphological as well as functional and hemodynamic data that have been proven indicative for reintervention and patient outcome. New MR techniques have been developed providing quantitative information of myocardial tissue characterization, deformation and 4-dimensional phase contrast (PC) imaging technique for advanced blood flow measurements with promising results to provide more refined indications for reoperations and interventions. This review will treat the current role of CMR in the diagnosis and follow up in TOF after repair involving the traditional MR sequences as well as new emerging techniques and their potential role in repaired TOF.

Keywords: Congenital heart defect; magnetic resonance imaging; tetralogy of Fallot (TOF); surgery

Submitted Aug 15, 2024. Accepted for publication Dec 30, 2024. Published online Feb 25, 2025.
doi: 10.21037/cdt-24-378
View this article at: https://dx.doi.org/10.21037/cdt-24-378

^ ORCID: Frida Dangardt, 0000-0003-4632-3916; Charlotte de Lange, 0000-0002-5990-1781.

Introduction

Tetralogy of Fallot (TOF), being the most common cyanotic congenital heart defect, has gone improved from grim to a favourable prognosis during the 20th century. Before the introduction of modern surgical techniques and perioperative care, children born with TOF rarely reached adult age and had a poor quality of life. Nowadays the long-term prognosis is excellent and many patients reach at least their 50s, and with a 30-year survival of >90%, albeit with lifelong needs for follow up and reintervention (1-4). There are still substantial challenges remaining such as the debate over how and when the total repair should be performed, where the initial treatment with the more traditional transannular patch (TAP) repair stands against the new valve sparing techniques. There is also a longstanding and ongoing discussion about the optimal timing for reintervention, where the imaging techniques available come into play; echocardiography, computed tomography (CT) and cardiovascular magnetic resonance (CMR) imaging. Although several imaging modalities are available, CMR is the most comprehensive and has evolved rapidly during recent years. This review will focus on how CMR can aid the decision-making regarding diagnosis and reintervention, how it can give a thorough assessment of right ventricular (RV) health, which is a broad concept encompassing more than ventricular volume and systolic function. Furthermore, by what means CMR may contribute to making a reliable prognosis for the individual patient with repaired TOF (rTOF) using both state-of-the-art traditional and recently developed and quantitative CMR techniques.

Pathophysiology of TOF and primary surgical treatment

The hallmark of TOF is the right ventricular outflow tract obstruction (RVOTO), which can occur at multiple levels; subvalvular, valvular and/or supravalvular. TOF is considered a tetrad of anomalies where the origin is an anterior misalignment of the infundibular septum with the muscular septum and the resulting RV hypertrophy, the ventricular septal defect (VSD) and the aorta over-riding the VSD. Small size of the branch pulmonary arteries is also common.

The level of cyanosis determines whether the infant needs immediate surgery during the neonatal period. There is an ongoing debate whether the staged approach, where the first step is a palliative procedure later followed by a definitive repair, or a primary repair is most favourable (5,6). Both strategies have their advantages; the neonatal repair is a more extensive procedure associated with morbidity at an earlier time, but it reduces the duration of cyanosis. The staged approach on the other hand does not expose the child to cardiopulmonary bypass during the neonatal period, which is a vulnerable period from a neurodevelopmental point of view, but there is a risk of shunt-related complications in the time interval until the complete repair (7-9).

The first step in the staged approach has historically consisted of a systemic-to-pulmonary shunt, originally the Blalock-Thomas-Taussig-shunt or a modification of it, but nowadays there is also a choice of stenting of the ductus arteriosus and balloon dilatation with or without stenting of the right ventricle outflow tract (RVOT) (10). The catheter-based alternatives are in most centers relatively uncommon; they are technically challenging and pose a risk of tricuspid valve damage during the procedure (11).

The objective of placing the shunt is to allow pulmonary arteries to grow, ensuring enough pulmonary blood flow until the patient can safely undergo the total repair; in most centres between the ages of 3 and 6 months (*Figure 1*). The total repair includes closing the VSD and reduces the RVOTO using either the TAP technique or valve sparing methods, and augmentation of branch pulmonary arteries when needed. The TAP leaves the pulmonary valve (PV) incompetent with ensuing pulmonary regurgitation (PR). The valve-sparing techniques on the other hand are not suitable for all patients, due to differences in the valve and RVOT morphology (12,13). The choice between these methods is based on institutional preference, surgical experience and the size of the PV and RVOT (14).

Imaging in the neonatal period relies heavily on echocardiography and this is in most cases sufficient for preoperative assessment. However, the patients with more complicated forms of TOF e.g., with major aortopulmonary collateral arteries (MAPCAs), often need additional imaging. CMR is feasible also in neonates, but in clinical practice, CT is often the method of choice, as it is a rapid examination mostly without need for sedation, and gives excellent detail of small vessels. It is also the first choice for shunt-related complications, for the same reasons as stated above, but also safer in a situation with an unstable patient.

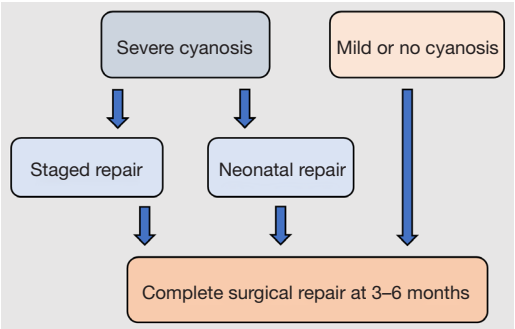


Figure 1 Algorithm for surgical intervention in new-borns with tetralogy of Fallot with mild or severe cyanosis.

Clinical assessment and treatment of late complications

Many patients with TOF who have undergone surgical repair live with chronic PR, which eventually leads to RV overload and dilatation. In the long run RV dysfunction occur with symptomatic decline and even left ventricle dysfunction which all contribute to increase the risk for arrhythmias and sudden cardiac death (15).

The resulting clinical symptoms of these complications are variable depending on the severity, and presenting with signs including palpitations, exertional dyspnea, exercise intolerance, syncope and signs of right heart failure (such as peripheral oedema, ascites, elevated jugular venous pressure and hepatomegaly). During the physical examination in older children and adults, a diastolic murmur may indicate PR, an ejection click, or a large "A wave" in the jugular venous pulse tracing could suggest RV dysfunction.

PR is one of the most common long-term complications after TOF repair in children and adults, particularly when a TAP is used as repair. Severe PR can lead to a progressive RV dilatation, dysfunction and further LV decline. Related symptoms include tricuspid valve regurgitation, which is often seen in severe RV dilatation. Additionally, the patients treated with RV-pulmonary artery (PA) conduits or valve sparing surgery face the risk of pulmonary stenosis (PS) and subsequent RV hypertrophy. However, PR is one of the most important haemodynamic factors predicting sudden cardiac death and consequently demands treatment (15).

Pulmonary valve replacement (PVR) is performed to prevent or improve the RV dysfunction and can be achieved either with an RV-PA conduit or by using transcatheter technique and a bioprosthetic valve. The timing of the PVR is a matter of discussion; there are criteria based on symptoms and RV end diastolic and end systolic volumes (16) (*Figure 2*). Finding the optimal time point for treatment is a fine balance between surgical risks and threat of irreversible damage to the right ventricle remains to be defined (17-19).

Atrial and ventricular arrhythmias are common in adults with rTOF, potentially leading to sudden cardiac death (20). Risk factors include atrial or ventricular surgical scarring, RV dysfunction. Electrophysiology studies and ablation, antiarrhythmic medications, or implantable cardioverter defibrillator (ICD) may be necessary to prevent or treat an underlying arrhythmia.

Patients with TOF are born with a relative dilatation of the ascending aorta which rarely leads to aortic root surgery, but warrants follow up (21).

In addition, especially adults with rTOF, are at increased risk for infective endocarditis in surgical patches, implants and prosthetic devices and requires antibiotic prophylaxis for certain dental or invasive procedures (22,23).

The above-mentioned complications in patients with rTOF evoke the need for surveillance and often repeated reintervention throughout their lifespan (24,25). Monitoring by multimodality imaging is important, with echocardiography as the primary imaging for assessing residual lesions, RV function and valvular status in adult rTOF, while CMR is considered the gold standard for quantifying RV size, function and PR. Cardiac catheterization may be necessary in order to evaluate the pulmonary vascular resistance, coronary anatomy and the severity of RVOT obstruction (20).

A structured multimodality follow-up is recommended at intervals specified in international guidelines for children and adults issued by the American Society of Echocardiography and the European Society of Cardiology (1,20).

Imaging in TOF

Echocardiography

The cornerstone in TOF and congenital heart disease (CHD) imaging is echocardiography, due to its low cost, availability, and absence of contraindications. It is non-invasive and offers detailed anatomical visualization as well as real-time functional assessment capabilities.

Transthoracic echocardiography (TTE) remains the primary imaging modality in the follow-up of patients with TOF. It allows for comprehensive evaluation of cardiac structures and function, assessing residual VSDs, RVOTO,

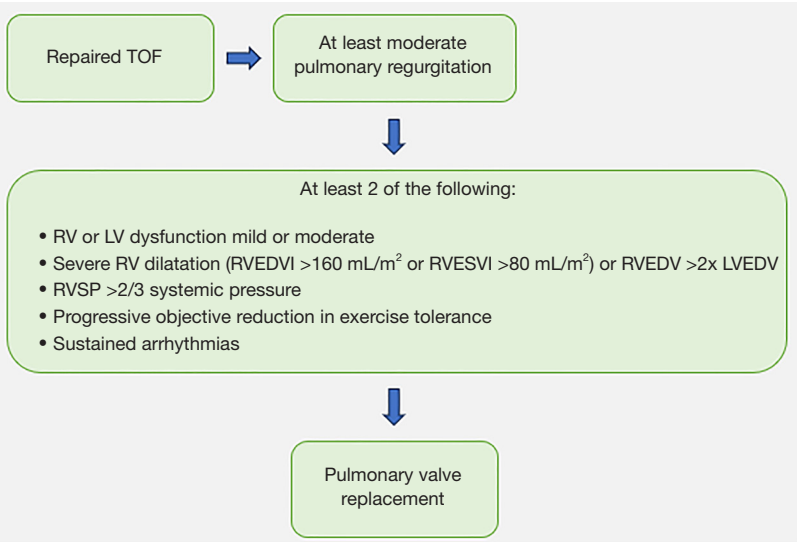


Figure 2 Algorithm for decision making in patients with repaired tetralogy of Fallot regarding pulmonary valve replacement, according to the 2018 American Heart Association/American College of Cardiology Guideline for the Management of Adults with Congenital Heart Disease (16). TOF, tetralogy of Fallot; RV, right ventricle; LV, left ventricle; RVEDVI, right ventricle enddiastolic volume index; RVESVI, right ventricle endsystolic volume index; LVEDV, left ventricle enddiastolice volume; RVEDV, right ventricle enddiastolic volume; RVSP, right ventricle systolic pressure.

RV hypertrophy, and aortic root dilation (26). Doppler techniques, including continuous and pulsed wave Doppler, are crucial for evaluating hemodynamic parameters. They are particularly useful for assessing the severity of residual PS and PR, both common issues in patients with rTOF. Newer techniques, such as three-dimensional echocardiography (3DE) offers enhanced spatial resolution, providing detailed visualization of complex cardiac structures such as the RVOT and pulmonary arteries. This modality is particularly useful for pre-surgical planning and postoperative evaluation, allowing for better assessment of RV volumes and function and a valuable technique when CMR is not available (27).

Advanced techniques like strain imaging, speckle tracking and tissue Doppler imaging provide detailed insights into RV mechanics and could be important for detecting subtle changes in RV function, and contrast agents can enhance endocardial border delineation and improve the accuracy of ventricular volume measurements, providing a more detailed assessment of RV function (27) (*Figure 3*).

Residual lesions such as VSDs, PR, and RVOT obstructions are common post-surgical complications.

Regular echocardiographic follow-ups are used for monitoring the progression of different lesions in TOF, as aortic dilatation as well as residual defects, valvular and ventricular dysfunction, and guiding therapeutic decisions, as well as determining when other imaging modalities such as CMR may be useful.

Cardiac catheterization

Catheterization also has a role in imaging of patients with TOF. The major advantage is the possibility to evaluate morphology as well as hemodynamics in addition to performing interventions, such as balloon dilation of a stenotic PV and stenting of persistent ductus arteriosus (PDA) or branch PA stenoses. Transcatheter-based alternatives for valve replacement are also an important part of the treatment options for patient in need of PVR. The other imaging modalities have almost completely come to replace cardiac catheterization when it comes to mere morphological and functional imaging, but sometimes invasive evaluation of hemodynamic parameters is warranted and cardiac catheterization is indispensable in these cases.

Computed tomography angiography (CTA)

Cross-sectional technique as CTA is indicated in the care of children with TOF, although predominantly for clinically

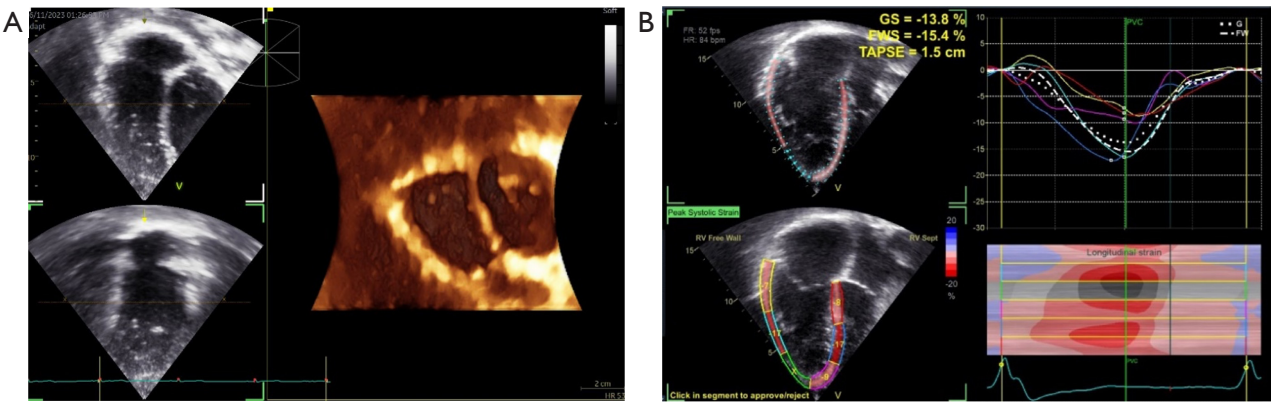


Figure 3 Advanced echocardiography techniques in TOF. (A) 3-dimensional echocardiography volume rendering-image of dilated right ventricle and normal sized left ventricle (colored image) of a 10-year-old girl with repaired tetralogy of Fallot. (B) Decreased global longitudinal strain in an 18-year-old boy with repaired tetralogy of Fallot. GS, global longitudinal strain; FWS, free wall strain; TAPSE, tricuspid annular plane systolic excursion; TOF, tetralogy of Fallot.

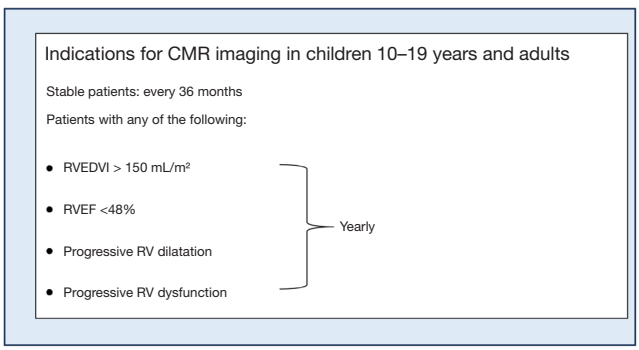


Figure 4 Recommendations from the American Society of Echocardiography, developed in collaboration with the Society of Cardiovascular Magnetic Resonance, the Society of Pediatric Radiology, and regarding follow-up for children and adults with repaired tetralogy of Fallot (1). CMR, cardiovascular magnetic resonance; RVEDVI, right ventricle enddiastolic volume index; RVEF, right ventricle ejection fraction; RV, right ventricle.

unstable children, in need of rapid preoperative anatomical assessment of the pulmonary and/or coronary arteries. In children as well as in adults, CTA might be the first choice in the presence of various contraindications to CMR, when monitoring postoperative complications in clinically instable patients (28). CTA including photon counting CTA, can be an important alternative when lumen in metallic implants or small structures like MAPCAs or fistulas need visualizing (29). However, patients with CHD are a relatively young patient group and will need follow-up imaging their entire life and therefore it is important to abstain methods with ionizing radiation, when possible, since patients with CHD have a higher risk of developing cancer (30).

CMR techniques and indications

CMR has evolved to become a robust, reproducible tool to evaluate the right ventricle, which is often difficult to fully visualise with echocardiography, and CMR is now the gold standard for RV evaluation providing data on end diastolic and end systolic volumes as well as stroke volume, ejection fraction and RV mass (1,31). The recommendations from the American Society of Echocardiography, developed in collaboration with the Society of Cardiovascular Magnetic Resonance and the Society of Pediatric Radiology, are that CMR should be performed only when echocardiography indicates an unfavourable disease progression in patients under 10 years of age (1,2). For older children, different intervals apply, while in asymptomatic adult patients with rTOF, the above guidelines suggest a follow-up interval of 12–36 months but with shorter intervals if clinical deterioration occurs (20) (*Figure 4*).

In accordance with present guidelines, the standard CMR protocol is more commonly performed on a 1.5T MR scanner due to less susceptibility artefacts in comparison to 3T, especially related to metallic implants, and to yielding more reproducible exams. However, when adjusting sequence parameters carefully, 3T can also be used achieving good image quality. In general, standard protocol (*Figure 5*) in begins with black blood single shot fast spin

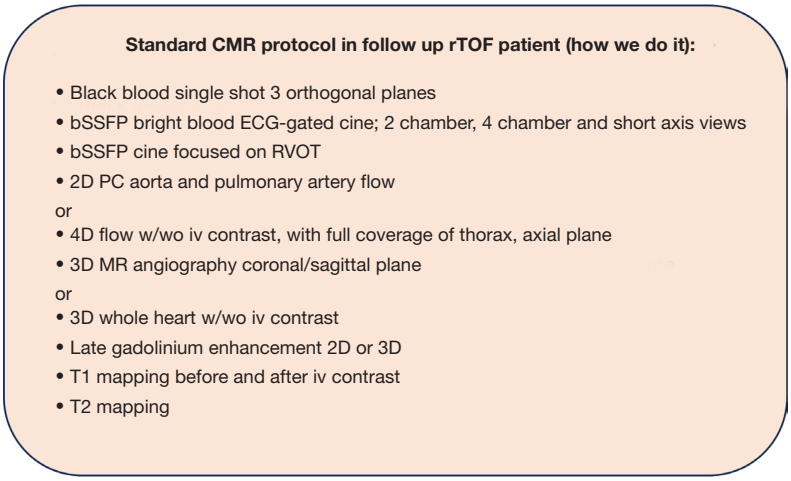


Figure 5 Clinical CMR protocol for follow up rTOF patients as performed in the authors' institution. CMR, cardiovascular magnetic resonance; rTOF, repaired tetralogy of Fallot; bSSFP, balanced steady state free precession; RVOT, right ventricular outflow tract; ECG, electrocardiogram; D, dimensional; PC, phase contrast; w/wo, with/without; iv, intraveneous.

echo or bright blood balanced steady-state free precession (bSSFP) based sequences for anatomical overview (2). The workhorse in CMR is evaluation of ventricular function using the bright blood electrocardiogram (ECG)-gated bSSFP cine sequences, which provides high contrast between blood and myocardium, acquired in the standard echocardiographic planes for volumetric assessment, myocardial thickness and for visualisation of regional and global systolic function. Specific cine images of the RVOT are often included. The 4-chamber view is useful for delineation of the atrioventricular valves and to visualise ventricular contractions (*Figures 6*,7).

Assessment of flow disturbances is an important part of the CMR evaluation in TOF and rTOF. In most centres, velocity encoded 2-dimensional (2D) phase contrast (PC) flow measurements are used to estimate the flow velocity in a vessel stenosis, to calculate regurgitant fraction in pulmonary insufficiency, and to assess residual shunts, flow in MAPCA's, tricuspid regurgitation and distribution of PA blood flow.

Flow measurements are adjusted to the expected vessel flow velocity as measured on echocardiography. 2D PC flow in the PA may vary during the respiratory cycle and should be performed in standardized way, and free breathing scans are used in many institutions (32) (*Figure* 7). PC measurements in the aorta and PA, or the sum of flow in the pulmonary branches can be used to estimate shunts with the Qp: Qs ["pulmonary stroke volume (L/min)/systemic stroke volume (L/min)"] in presence of residual VSD or other shunts. PC imaging in in the left and right pulmonary branches can quantify blood flow distribution between the lungs. Newer techniques like multidirectional PC 4-dimensional (4D) flow CMR can follow hemodynamic events during the cardiac cycle and flow measurements can be performed retrospectively in any desired plane (33,34). This is further discussed in the section below.

The 3D whole heart sequences, a 3D bSSFP sequence with both ECG gating and respiratory navigation, yields a bright blood full isotropic volume dataset over the mediastinum /thorax and used for vessel and intracardiac anatomic detail assessment; diameters of branch PA, the aortic root/aorta and excellent coronary anatomic detail can be evaluated (35,36) (*Figures 6-8*).

Finally, CMR can provide information on myocardial viability. The late gadolinium enhancement (LGE) sequence commonly performed as an inversion recovery gradient echo sequence requiring gadolinium-based contrast agents (GBCAs), is used to assess myocardial scarring and fibrosis. Adult patients with rTOF often have scarring related to areas of surgical repair (the TAP or VSD) and sometimes even in remote locations in the myocardium (*Figure 9*). Presence of more extensive myocardial fibrosis predominantly in the RV has been shown related to the increased risk of ventricular arrhythmia and sudden cardiac death (37,38) and can be important in decision making regarding ICD (20). As the cohort of patients with CHD is growing older, they can also be affected by acquired heart disease in which LGE imaging can reveal ischemic

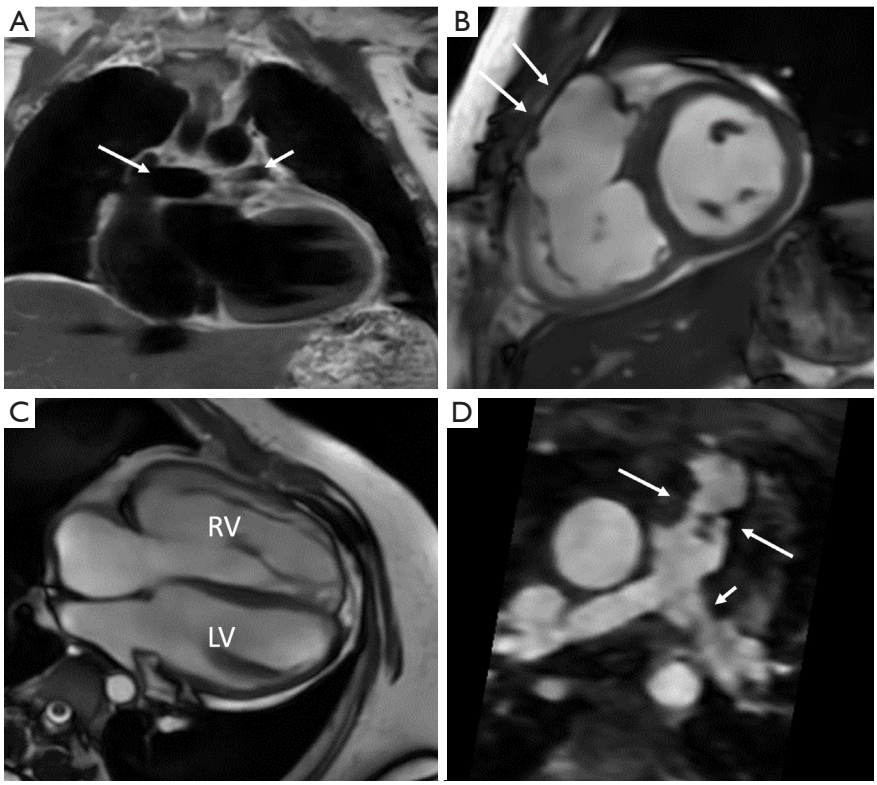


Figure 6 A 12-year-old boy with tetralogy of Fallot and pulmonary atresia, repaired with a conduit from right ventricle to pulmonary artery. CMR standard protocol performed to evaluate RV volume and function and PA anatomy. A 1.5 T CMR, black blood sequence for overview and anatomy, shows a narrow left pulmonary artery (short arrow) and normal size right pulmonary artery (arrow in A). A 2D bSSFP cine sequence in a short-axis view with a dilated right ventricular out flow tract/conduit (arrows in B). A 4-chamber view bSSFP cine sequence images with a dilated trabeculated (RV), and a normal sized LV (C). A 3D bSSFP in an oblique axial plane for anatomical details, where the irregular and calcified conduit (arrows) and narrow LPA are depicted (short arrow in D). RV, right ventricle; LV, left ventricle; CMR, cardiovascular magnetic resonance; PA, pulmonary artery; 2D, 2-dimensional; bSSFP, balanced steady state free precession; LPA, left pulmonary artery.

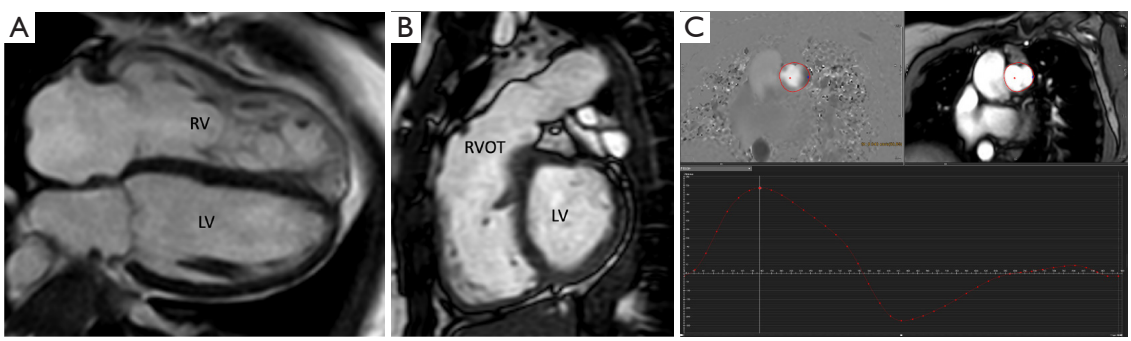


Figure 7 A 45-year-old woman with repaired tetralogy of Fallot with a transannular patch where echocardiography exhibit dilated RV and severe pulmonary regurgitation. Standard CMR protocol to evaluate RV volume and function, and flow measurements. (A) 1.5 T CMR, 2D bSSFP image in a 4-chamber view with dilated trabeculated RV as compared to the LV. (B) 2D bSSFP in an oblique view over the RVOT revealing slightly dilated and irregular borders of the pulmonary artery. (C) 2D phase contrast flow measurement traced above the pulmonary valve in the phase image (upper left) and the anatomic image (upper right) with flow curve (below) and a regurgitant fraction calculated to 40%. RV, right ventricle; LV, left ventricle; RVOT, right ventricular outflow tract; CMR, cardiovascular magnetic resonance; 2D, 2-dimensional; bSSFP, balanced steady state free precession.

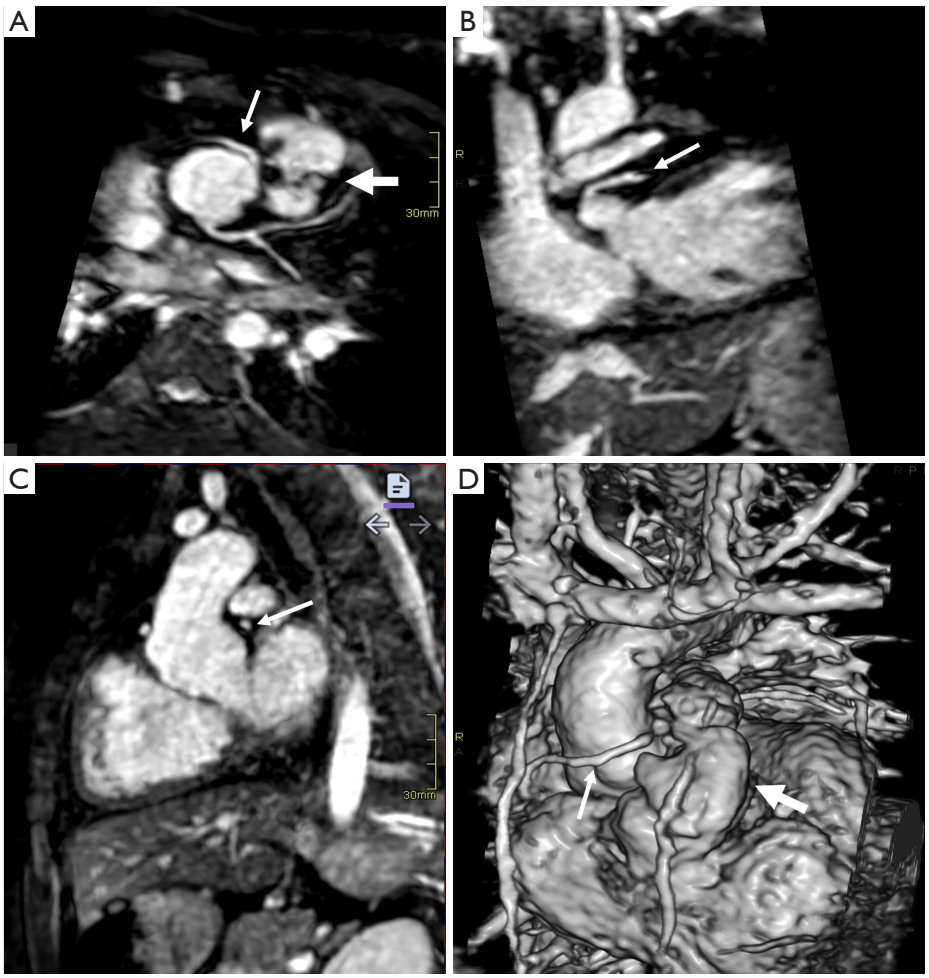


Figure 8 A 13-year-old boy with tetralogy of Fallot with pulmonary atresia and VSD repaired with a Contegra graft and VSD closure, now developing stenosis in the graft. CMR including 3D balanced steady state free precession with respiratory navigation and ECG triggering, was performed to evaluate the coronary anatomy for the treatment decision of pulmonary valve replacement. Multiplanar reconstructions are displayed in an axial oblique (upper left, A), a coronal oblique (upper right, B), sagittal oblique (lower left, C) views and a volume rendered image (lower right, D). There is a narrow, irregular and calcified graft (thick arrows in A and D). The aortic root is rotated to the left and the right coronary artery has a ventral course to the right crossing the aortic root and in the immediate vicinity to the graft. The left coronary artery, with the left descending artery passes only 1 mm behind and below the graft (arrows in B and C). A surgical valve replacement was decided for treatment since interventional stent implantation would implicate a high risk of injuring the coronary arteries during balloon dilatation of the graft stenosis. VSD, ventricular septal defect; CMR, cardiovascular magnetic resonance; 3D, 3-dimensional; ECG, electrocardiogram.

scarring. The use of GBCA is controversial due to the reported development systemic nephrogenic fibrosis related to impaired renal function. In addition, there are strategies to decrease use or avoid GBCA especially infants and young children due to its deposition of Gadolinium in especially the brain and with still unknown long-term effects (39,40). Nevertheless, studies have shown the safety with GBCA without adverse health events related to Gadolinium deposits in the brain (41). New technology with synthetic LGE imaging and MR fingerprinting (a single scan yielding T1, T2 values and tissue perfusion, diffusion, fat fraction and T2*), might overcome the use of GBCA.

Bloodpool agents as Ferumoxytol (off label use in many countries) might be used to enhance anatomy and provide comprehensive flow analysis, including 4D flow (42).

Different indications for pre- and postoperative

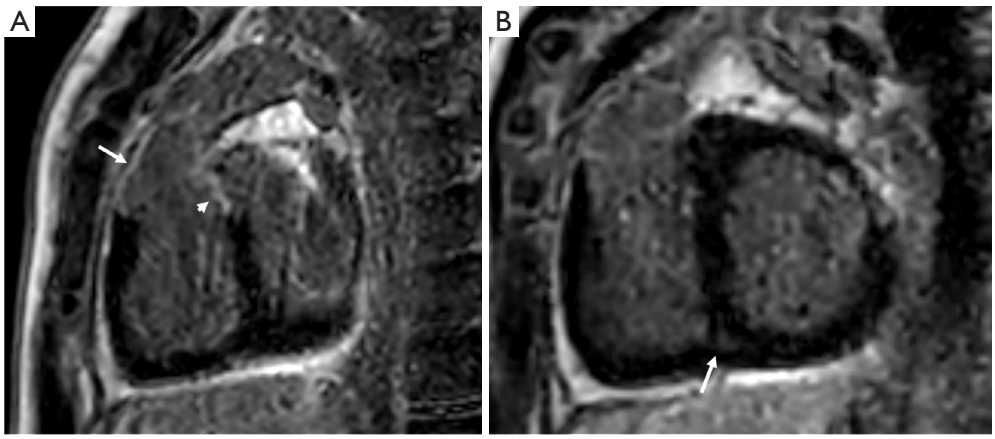


Figure 9 A 14-year-old girl with pulmonary atresia and VSD repaired with a conduit from the right ventricle to the pulmonary artery and a septal patch. A CMR performed to evaluate substrate for arrhythmia, with late gadolinium enhancement in contiguous short axis planes reveals (A) enhancement in the conduit in the outflow tract (long arrow) and in the ventricular septal patch (short arrow). (B) Enhancement shown in the inferior septal hinge point (arrow). VSD, ventricular septal defect; CMR, cardiovascular magnetic resonance.

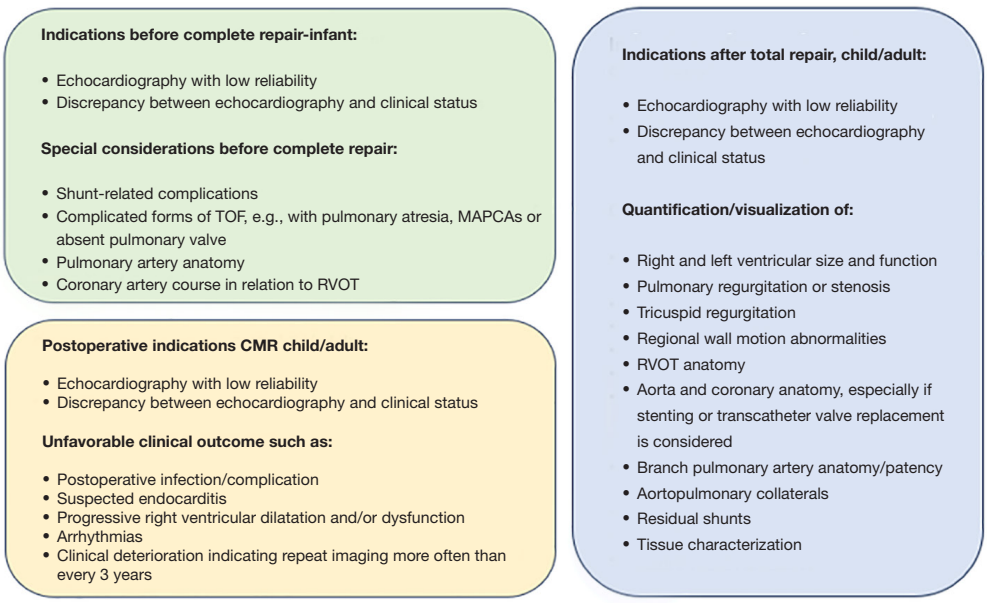


Figure 10 Indications for CMR in the pre- and postoperative setting, for infants with tetralogy of Fallot prior to and after total repair (rTOF), and for older children/adults with rTOF prior to and after pulmonary valve replacement respectively. TOF, tetralogy of Fallot; MAPCAs, major aortopulmonary collaterals; RVOT, right ventricular outflow tract; CMR, cardiovascular magnetic resonance.

investigation with CMR in TOF and rTOF according to age are shown in (*Figure 10*).

Pitfalls and challenges

The cornerstone in volumetric measurements in CHD is the 2D cine bSSFP in a short axis plane. However, these sequences can be challenging especially in children with the risk of artefacts due to multiple serial breath holds, thick slices with less anatomical detail with malalignment of consecutive slices, that all introduce an uncertainty volumetric measurement. New techniques using fast

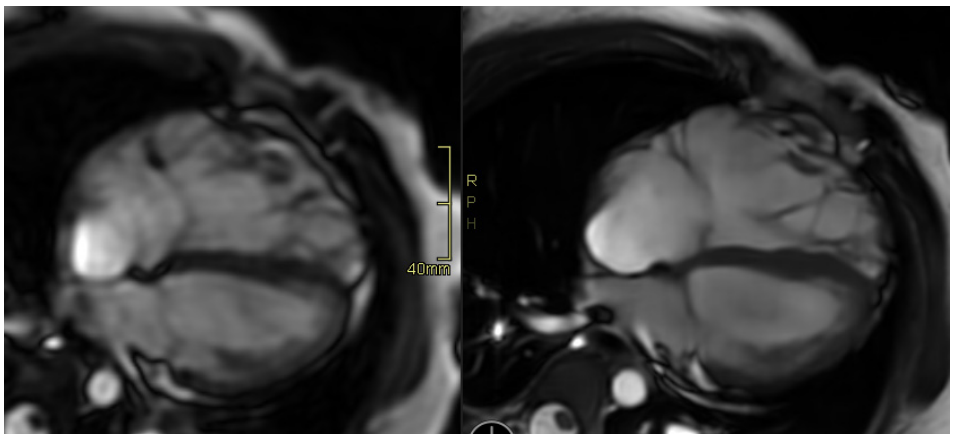
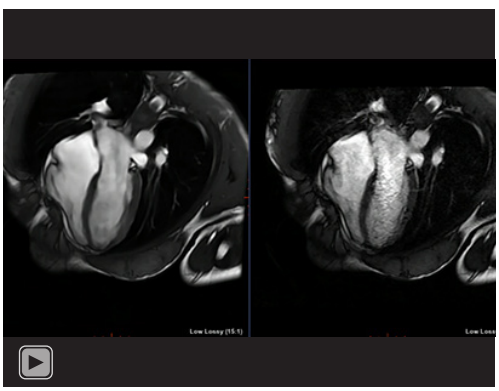


Figure 11 A 12-year-old boy, the same patient as in *Figure 5*. CMR standard protocol performed to evaluate RV volume and function. Illustration to compare image the resolution. A 2-dimensional bSSFP cine images in a 4-chamber view, with and without acceleration, performed in free breathing. Conventional cine bSSFP (left), and cine bSSFP acquired with highly accelerated single heartbeat, reconstructed with deep learning revealing increased sharpness in delineation of myocardial borders and papillary muscles (right). Cine sequence in a 4-chamber view seen in *Video 1* (conventional cine to the right and cine with deep learning to the left). CMR, cardiovascular magnetic resonance; RV, right ventricular; bSSFP, balanced steady state free precession.



Video 1 A 12-year-old boy, the same patient as in *Figure 5*. CMR was performed to evaluate the RV volume and function. Illustration to compare image resolution. A 2-dimensional bSSFP cine images in a 4-chamber view, with and without acceleration, performed in free breathing. Conventional cine bSSFP (right video), and cine bSSFP acquired with highly accelerated single heartbeat, reconstructed with deep learning revealing increased sharpness in delineation of myocardial borders and papillary muscles (left video). CMR, cardiovascular magnetic resonance; RV, right ventricle; bSSFP, balanced steady state free precession.

accelerated deep learning in 2D cine bSSFP and isotropic fast free-breathing time resolved 3D cine sequences or achieved in one breath hold, as well as compressed sensing techniques, have the potential to overcome or ameliorate these problems. These techniques provide shorter scan times, 3D image reconstruction using parallel imaging, deep learning post-processing, faster acceleration techniques with motion correction and higher image resolution (*Figure 11*, *Video 1*) (43). This is especially important in smaller children to achieve volumetric short axis cine images with more reliable and reproducible measurements of ventricular volumes, as being an important part in rTOF monitoring with CMR.

Flow quantification as mentioned, is routinely used in CMR and is validated as a reliable and reproducible technique in large vessels (44). Nevertheless, regarding small caliber vessels, flow quantification requires special attention in 2D as well as in 4D flow, since the small vessel area may overestimate the correct flow due to partial volume effect and consequently requiring post-processing correction. This is of importance especially in small children, when measuring flow in the pulmonary arteries which is often required in CHD and rTOF for perfusion ratio calculation (45).

Metallic implants and stents require special considerations as mentioned in the above section. Patients with rTOF with cardiac implantable electrical devices (CIED) are frequently in need of a CMR evaluation. It has been shown lately that MR in most cases can be performed safely in a 1.5T scanner even in children, by using appropriate protocols adherent to safety guidelines. In each individual case a thorough risk—

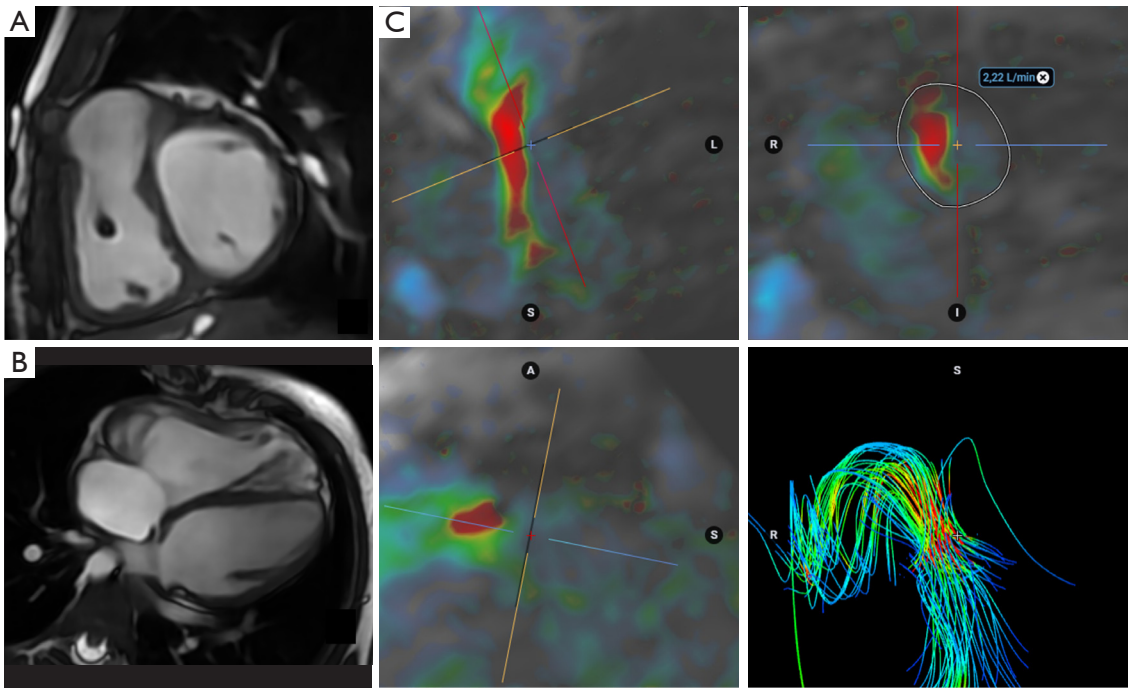


Figure 12 A 6-year-old boy with repaired tetralogy of Fallot with pulmonary atresia and ventricular septal defect. After correction he developed a pseudoaneurysm and was reoperated with a new transannular patch. CMR to evaluate his enlarging right ventricle and pulmonary regurgitation. The examination was performed without anesthesia and the patient received a sedative but was nevertheless fully awake and had his parent with him in the scanning room. The scanning was kept very brief and instead of a short axis stack through the ventricles, only a 2-dimensional balanced steady state free precession cine sequences was performed (A), where the large right chamber and dilated right ventricular outflow tract are clearly visualized. The 4-chamber view (B) depicts a large right ventricle. (C) 4-dimensional flow was performed with a scan time of 4.5 minutes and without iv contrast. Flow in the pulmonary artery is seen in 3 planes and streamlines with flow in both antegrade and retrograde direction is shown in systole. CMR, cardiovascular magnetic resonance; iv, intraveneous.

benefit assessment must be done prior to the scanning, and CMR with a CIED is never a routine exam (46,47).

Due to their small size, children require images with high spatial resolution. In that regard it may be an advantage to use 3T CMR to achieve optimal anatomical detail, even though the risk for susceptibility artifacts is increased. Breath hold sequences are difficult for children and sometimes even for adults, and here adapted free breathing sequences using deep learning techniques are now widely available (*Figure 11*, *Video 1*). In addition, avoiding breath holds also minimizes the need for general anaesthesia with intubation (48). Infants generally need some kind of sedation; in many cases feed-and-wrap or a mild sedation with preserved spontaneous breathing is sufficient (49). For children with indication for a longer CMR protocol or where close haemodynamic surveillance is warranted, general anaesthesia is the preferred option. Before scanning, the most important sequences need to be identified and prioritized, if the examination is interrupted by an awakened child (48). From the age of 6–7 years a short protocol CMR can often be performed awake while listening to music or watching film in the scanner (*Figure 12*). Prior to the scanning, a study visit may be beneficial, to make the child acquainted with the MR lab and the examination setting (50).

Advanced CMR techniques in repaired TOF

The traditional CMR techniques with criteria used in the evaluation of PVR have insufficient reliability in predicting postoperative ventricular arrhythmia, heart failure, and sudden cardiac death. Thus, a more advanced and comprehensive myocardial and hemodynamic evaluation is desired identifying RV (dys)function in TOF and rTOF. CMR imaging "biomarkers" for prediction of disease progression have recently been developed including

four-dimensional phase-contrast imaging (4D flow), strain analysis with tissue tracking and myocardial tissue characterization using parametric mapping techniques, which are now established in clinical practice. The clinical impact in CHD of these techniques has been demonstrated in several studies and recent guidelines recommend them to be included in CMR reporting for CHD and rTOF (2,51-53). Other emerging sequences and post-processing techniques relevant for rTOF are still under research such as diffusion tensor imaging (DTI) and CMR elastography and computational fluid dynamics, but not set for clinical use.

Four-dimensional flow CMR

4D flow CMR is a development of the traditional 2D PC imaging and has proven particularly important in the evaluation of CHD and pediatric patients (54). This sequence provides quantitative evaluation of flow in an entire volume within the thorax with velocity-encoding in all three spatial directions throughout the complete cardiac cycle. Flow velocity and flow volume acquired with 4D flow have been validated against 2D PC flow in TOF (33,34). As a real-time respiratory gated assessment throughout the respiratory cycle, 4D flow enables the same diagnostics as can be evaluated with techniques in echocardiography and now photon counting CT (55,56). Technical development has resulted in decreased scanning times for 4D flow and is now typically performed in 5–10 min covering the thorax and can be performed with both 1.5 and 3T scanners (54). The spatial resolution will be superior by 3T scanning where adding GBCA will further enhance the anatomical delineation. Using commercially available software, analysis of data on flow volumes, velocities, flow patterns, as well as more advanced hemodynamic parameters as wall shear stress and calculation of kinetic energy loss and vortex visualization with insights into the complex hemodynamics, are retrospectively retrieved. They provide direct quantification of valve and vessel stenosis, pulmonary hypertension and aortic coarctation even in neonates and offers the possibility to differentiate multiple intracardiac shunts (54,57) (*Figures 13,14*).

Quantification of PR holds particular importance in the timing of PVR (17) and 4D flow has better spatial coverage in all dimensions enabling visualization of flow jets and streamlines through stenotic valves and could thereby potentially provide novel criteria for PVR in these patients (58) (*Figures 13,14*, *Videos 2,3*). Furthermore, 4D flow CMR may also enable precise measures of RV diastolic function including data from analysis of the caval vein, tricuspid valve, and pulmonary blood flow profiles (33,54,58,59).

Careful adjustments in the sequence settings and adaptation to patient size, scan coverage as well as applying velocity encoding according to expected flow velocities is important as in 2D PC. The 4D flow has a special advantage in more complex cases where multiple quantitative measurements on both venous and arterial sides are needed (60-62).

Tissue characterization

CMR provides the possibility to detect changes in tissue composition in the myocardium, such as diffuse fibrosis, scarring, edema, fat and iron deposition by the intrinsic T1 relaxation properties in fibrosed, scarred myocardium or LGE and extracellular volume (ECV) fraction.

LGE

Repaired TOF, is the only CHD where LGE extent has been shown to independently predict mortality (37) as rTOF is associated with decreased biventricular EF, RV dilatation, poor functional class and exercise intolerance and mortality (63,64). Furthermore, visual grading of LGE presence and direct quantification of LGE extension has been reported in adult rTOF studies related to RV systolic dysfunction, dilatation and atrioventricular arrhythmias (38,65,66). Further to the development with free breathing 3D gradient echo-based LGE sequences can improve scar detection and quantification also reported in rTOF (66). This technique might potentially better detect arrhythmogenic anatomic sites available for ventricle tachycardia ablation (67).

T1, T2 mapping

Quantitative measures of tissue characterization with CMR derived T1 and T2 mapping allows for the detection and grading of diffuse myocardial fibrosis, also in CHD (68,69), as well as edema and inflammation. T1 parametric mapping rely on the generation of images at different degrees of longitudinal relaxation to generate a signal intensity vs time curve from which T1 is calculated. The most common sequence is the modified Look Locker inversion recovery sequence (MOLLI) or the shortened MOLLI (ShMOLLI) with reduced time of breath hold (70,71). Acquisitions pre- and post-contrast injection allows for calculation of the ECV fraction.

Elevation of native T1 values in the LV and ECV have been

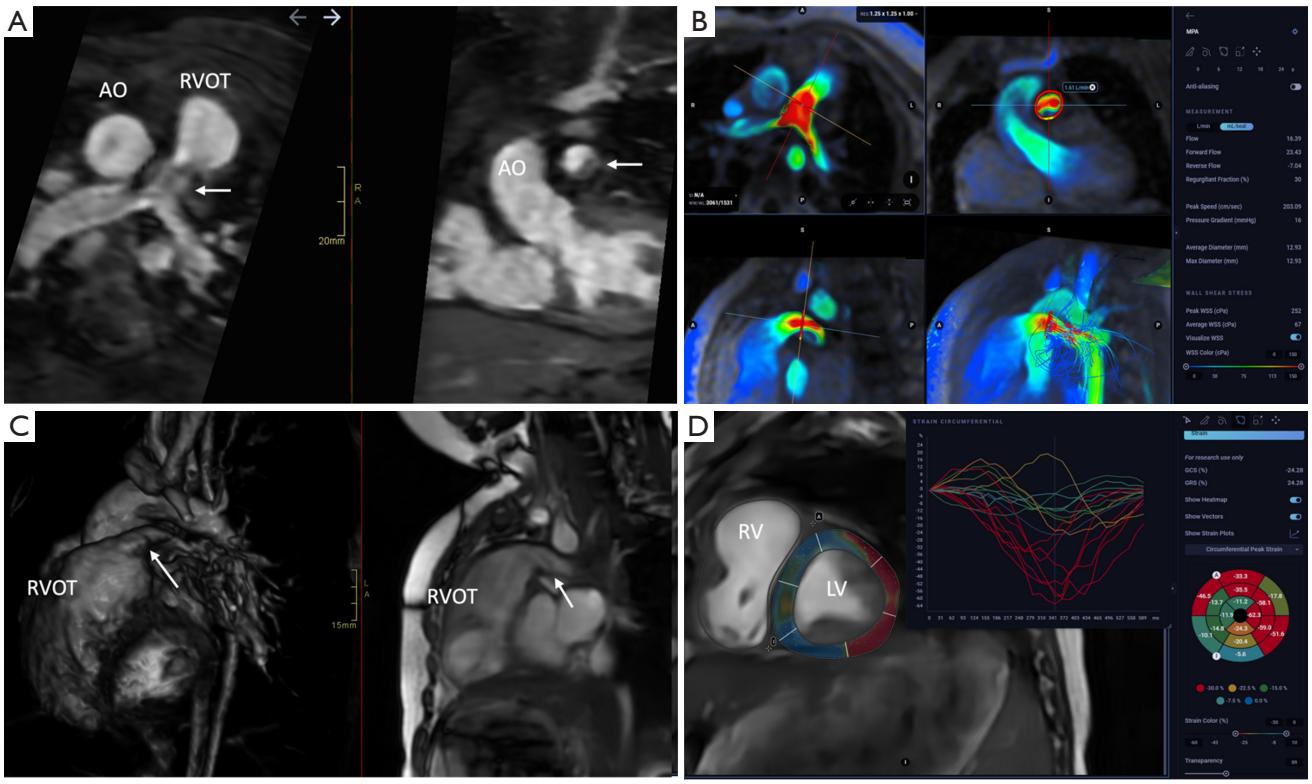


Figure 13 A 20-month-old girl with repaired tetralogy of Fallot with a conduit from right ventricle to pulmonary artery and a left pulmonary artery stenosis plasty. 3T CMR free breathing performed in dexmedetomidine sedation, for basic and advanced analysis with pulmonary perfusion ratio. (A) MPR of 3D bSSFP in an axial and coronal plane showing dilated RVOT and a narrow pulmonary conduit (arrows). (B) Software analysis of 4D flow with MPR and volume rendering of the pulmonary artery/conduit with streamlines. Pulmonary artery peak velocity 2.05 m/s and a regurgitant fraction of 30%. Pulmonary perfusion of 70% to the right lung (red color represents high and blue color low velocity). (C) 2D cine bSSFP (right) and volume rendering of the 3D bSSFP in a sagittal oblique plane showing the dilated RVOT and narrow small conduit. (D) 2D cine SSFP in a short-axis view for volumetric analysis revealing an increased end diastolic volume of the right ventricle of 115 mL/m^2 and ejection fraction of 47%. Radial and circumferential strain analysis of the left ventricle showing impaired strain curves in the septum and basal inferior wall, underlined in blue and green color in the curves and short axis view of the myocardium. AO, aorta; RVOT, right ventricular outflow tract; RV, right ventricle; LV, left ventricle; CMR, cardiovascular magnetic resonance; MPR, multiplanar reconstruction; 3D bSSFP, 3-dimensional balanced steady state free precession; 4D, 4-dimensional.

introduced as possible risk markers for rTOF both in children and adults, with important predictive information for rTOF outcome and associated with abnormal pre-or afterload, longer cardiopulmonary bypass times, chronic hypoxia and genetic factors. In rTOF increased LV T1, ECV are associated with abnormal strain and ventricular arrhythmias (38,59,65,72) (*Figure 15*). T1 mapping in the thin RV wall is challenging with the standard LV T1 mapping technique. However, increased RV T1 values have been shown correlated with increased RV volume and severity of PR (59,65).

T2 mapping similarly relies on fitting of a curve of signal intensity values on different times during transverse relaxation and offers a more objective detection and quantification of myocardial edema and inflammation than edema sensitive sequences and may be important in rare complications of rTOF as acute myocarditis, and in other situation such as infarction heart transplant rejection or dilated cardiomyopathy (73).

Myocardial strain

Myocardial deformation, called '*myocardial strain*', derived from standard cardiac MR sequences deduced from 2D-CMR feature tracking, is an additive post-

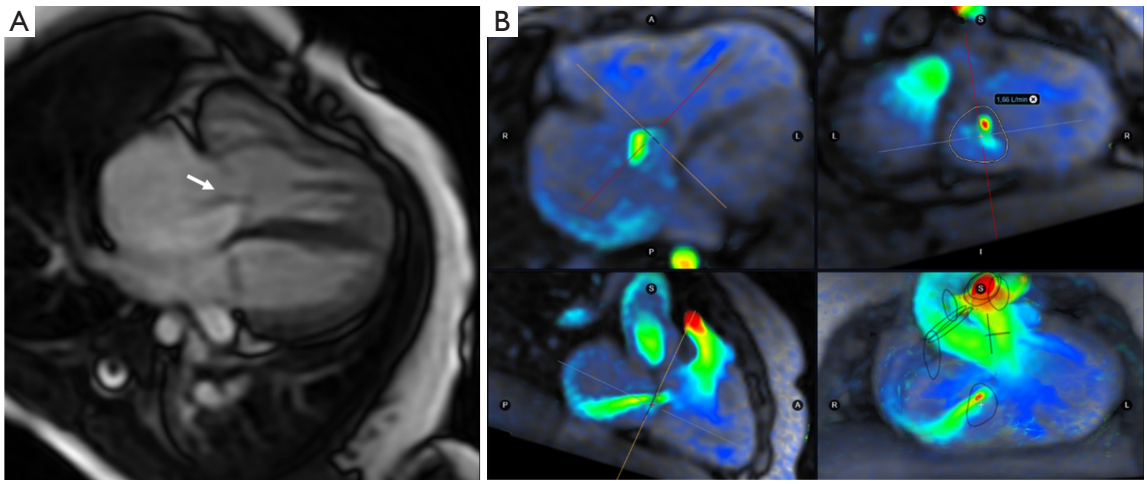
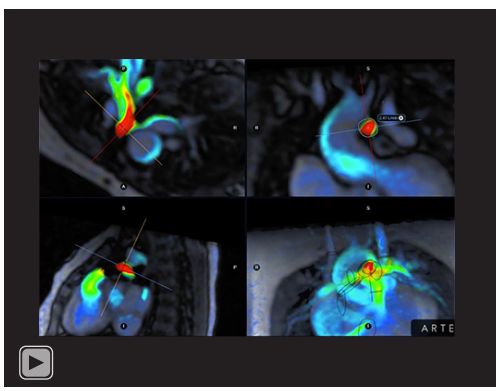
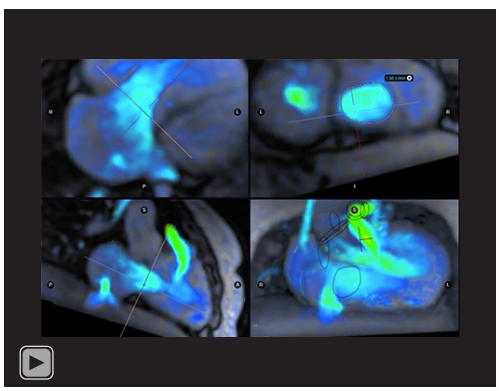


Figure 14 A 5-year-old girl with tetralogy of Fallot and a pulmonary artery conduit with stenosis and pulmonary regurgitation. A 1.5 T CMR performed in sedation with dexmedetomidine and free breathing, can evaluate right ventricle dilatation and hypertrophic wall and pulmonary regurgitation. On 4D flow sequence pulmonary regurgitation and velocity is visualized and measured posterior to pulmonary conduit (*Video 2*) (red color represent high velocity and blue, low velocity). A tricuspid regurgitation visualized on cine 4-chamber view (arrow in A). The 4D flow can better visualize the eccentricity of the regurgitation jet towards the atrial wall (crosshair in B) and allow calculation of the regurgitant fraction to 20% (*Video 3*). CMR, cardiovascular magnetic resonance; 4D, 4-dimensional.



Video 2 A 5-year-old girl with tetralogy of Fallot and a pulmonary artery conduit with stenosis and pulmonary regurgitation. The same patient as in *Figure 14*. A 1.5 T CMR performed in sedation with dexmedetomidine and free breathing, can evaluate right ventricle dilatation and hypertrophic wall and pulmonary regurgitation. On 4D flow sequence pulmonary regurgitation and velocity is visualized and measured posterior to pulmonary conduit (red color represent high velocity and blue, low velocity). CMR, cardiovascular magnetic resonance; 4D, 4-dimensional.



Video 3 A 5-year-old girl with tetralogy of Fallot and a pulmonary artery conduit with stenosis and pulmonary regurgitation. The same patient as in *Figure 14*. A 1.5 T CMR performed in sedation with dexmedetomidine and free breathing, can evaluate right ventricle dilatation and hypertrophic wall and pulmonary and tricuspid regurgitation. A 4D flow (red color represent high velocity and blue, low velocity) of the tricuspid valve. The 4D flow can visualize the eccentricity of the regurgitation jet towards the atrial wall (lower left image). CMR, cardiovascular magnetic resonance; 4D, 4-dimensional.

processing technique for sensitive evaluation of myocardial deformation in longitudinal, circumferential and radial planes. CMR strain has recently been reported to predict adverse outcomes for patients with rTOF (63) revealing ventricular dysfunction in aortic valvular disease with preserved function in adults (74). Myocardial strain is

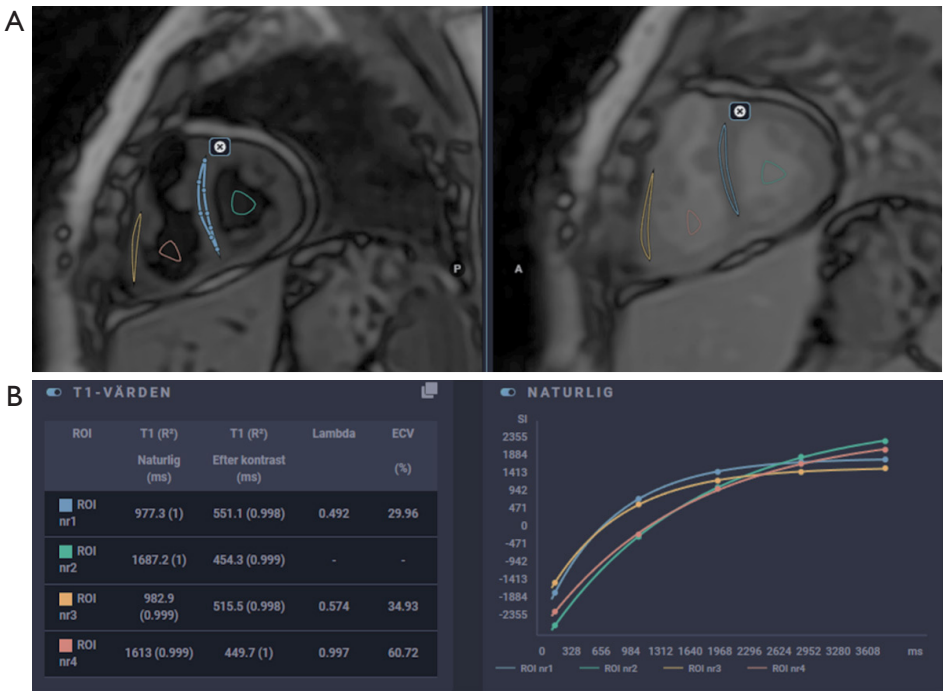


Figure 15 Evaluation of diffuse myocardial fibrosis in a 5-year-old girl with tetralogy of Fallot and left branch pulmonary stenosis repaired with a pulmonary graft later on dilated with a stent with recurrent stenosis and pulmonary regurgitation (the same patient as in *Figure 14*). (A) A 1.5T CMR, free breathing T1 mapping, ShMOLLI, with deep learning algorithm in a midventricular short axis plane. Software analysis with manually traced regions of interest on pre- (left) and post-contrast images (right). (B) Corresponding values (left) and relaxation curves (right). Native T1 977 ms in the septum and 982 ms in the right ventricular wall, corresponding to values within the locally established normal range for this scanner. Slightly increased extracellular volume fraction of 29.6% in the septum. ROI, region of interest; ShMOLLI, shortened modified Look Locker inversion recovery; CMR, cardiovascular magnetic resonance.

analogue to echocardiographic strain and utilizes traditional cine sequences in short axis and longitudinal plane, to identify RV and LV ventricular contraction patterns that might be of importance for early disease prediction and major adverse cardiac events (75). Post-processing identifies small geometric structures or features, in all frames during the cardiac cycle (*Figure 13D*). Displacement is calculated in % or strain rate 1/strain from the baseline and reported in global, segmental, and local myocardial function according to the formula: (L1 – L0 or L)/L0, where L0 is the initial tissue measurement (usually in end diastole) and L1 is the final tissue measurement (in end systole) (76). Reference values are published for adults and for pediatric age and weight groups (77-79).

Cardiac magnetic resonance perfusion/ stress perfusion

In perfusion CMR a bSSFP sequence is performed while the first pass perfusion of GBCA is sampled during the cardiac cycle in different planes simultaneously (53). Perfusion can be studied at rest or under induced stress, the latter with physical exercise using an MR compatible ergometer or more often with pharmacological drugs such as dobutamine or adenosine. CMR perfusion is established and widely used in acquired heart disease. Stress perfusion is less frequent in CHD, although shown to be a safe technique to use also in pediatrics (80). Indications in CHD patients with RV or single ventricle circulation are evaluation ventricular functional parameters such as wall motion and in suspected coronary pathology in CHD or acquired cardiac disease or in combination with exercise testing. This could typically be in the evaluation of inducible ischemia in Kawasaki disease, postoperatively in transposition of the great arteries with reimplantation of the coronary arteries and may be indicated in rTOF to evaluate ischemia and RV function under stress (81).

Other techniques under development for cardiac use

The CMR technology is under constant development following the clinical demands and new treatment options. Some sequences are further developed finding new applications in other organs and new CMR biomarkers enabling quantification of physiological processes can potentially allow for a more personalized treatment that can be important in CHD and rTOF.

In MR elastography, the propagation of shear wave speed is measured to quantify tissue stiffness, as a surrogate for fibrosis. This method is especially established in staging liver fibrosis in chronic liver disease (82). Ultrasound shear wave elastography in cardiology is increasingly used in clinical studies (83). Elevated myocardial stiffness causes poor function and restrictive diastolic filling that can lead to heart failure, even with a normal left ventricular ejection fraction. Myocardial left ventricle CMR elastography has shown promising results revealing increased myocardial stiffness related to cardiac failure but also that stiffness seems to increase with natural aging and especially in females (84,85). No experience in rTOF so far.

DTI is widely used in brain imaging. In the myocardium, DTI displays the diffusion of water within the myocardial matrix. The measures of the so-called eigenvectors correspond to the arrangement of left ventricular cardiomyocytes and are validated to histology (86). Sequence development now allows for acquisition of the beating heart to study the micro architecture in ischemic hypertrophic cardiomyopathy. DTI may improve prognostic assessment of myocardial remodeling although still not technically ready to investigate the RV thin wall.

Risk stratification of repaired TOF with imaging

Risk stratification in patients with repaired TOF is crucial for optimizing long-term outcomes and guiding management strategies. CMR together with echocardiography plays a pivotal role in this process by providing detailed assessments of cardiac anatomy and function, detecting complications, and helping predict adverse events. Other diagnostic modalities are also important for risk stratification, such as evaluation of cardiopulmonary exercise capacity (CPET) or arrhythmias by exercise testing or ambulatory ECG monitoring for example (37). Several studies in adults with rTOF attempt identification of patients at high risk for premature death or malignant arrhythmias. Most often, a multi-modality diagnostic approach has been used.

CMR, plays an essential role, and has been found to provide several important, independent risk factors for mortality such as PV and RVOT dysfunction, RV hypertrophy, reduced RV or LV ejection fraction, as well impaired strain and LGE extent in both the RV and LV (37,87,88).

Echocardiography is used in risk stratification mainly to get an indication of the function and volume of the ventricles. In children, RV area is an acceptable echocardiographic parameter to screen RV dilation as compared with CMR, and doppler may be used for evaluating and grading the severity of PR (89). Using novel methods in echocardiography such as myocardial deformation as measured by strain has also improved the risk assessment in these patients. Patients with lower longitudinal strain (LS) in either the LV or RV has been shown more likely to die or develop heart failure, even if only RV free wall LS maintained a significant association with outcomes after adjustments (90). Additionally, multiple studies have shown that both left atrial and right atrial mechanics are impaired in this population (91). Specifically, abnormal atrial compliance has been associated with a history of life-threatening arrhythmias in individuals with rTOF (18) and an increased atrial area as measured by CMR has been shown to independently predict clinical atrial and ventricular arrhythmia (92).

One of the largest prospective risk assessment studies to date included 873 patients with rTOF and a median age of 24 years, in which almost 4% reached the primary outcome of death or sustained ventricular tachycardia (VT). The best predictive model found in that study included RV mass-to-volume ratio ≥0.3 g/mL, LV EF z score <–2.0 (<55% in males and <54% in females), and history of atrial tachyarrhythmias. In patients with none of those predictors, freedom from the outcome was 98% at 5 and 10 years. Another recent retrospective multicenter study of 1088 patients could demonstrate that RV EF ≥42% and RV mass index <39 g/m^2 consisted a low risk for major adverse clinical outcomes after age 50 years (87,88).

LGE can detect focal myocardial fibrosis, which is linked to both ventricular arrhythmias and sudden cardiac death. In a study of 550 patients with rTOF, (median age 32 years, 27 deaths) RV LGE burden, presence of LV LGE, RV ejection fraction ≤47%, LV ejection fraction ≤55%, B-type natriuretic peptide ≥127 ng/L, peak exercise oxygen uptake (VO_2) ≤17 mL/kg/min, prior sustained atrial arrhythmia, and age ≥50 years all independently predicted mortality (37). Diffuse fibrosis as measured by increased T1 mapping in patients with rTOF, have gained increasing interest since fibrosis possibly is a reversible process. Studies

have shown increased T1 in the RV and LV being linked to adverse markers of outcome and events (37,93).

While not being imaging modalities, ECG and Holter monitoring are essential in the risk stratification of arrhythmias. Prolonged QRS duration (>180 ms) on ECG is a marker of increased risk for ventricular arrhythmias and sudden cardiac death in patients with TOF. Holter monitoring can detect asymptomatic arrhythmias that may require intervention (27). Exercise testing, especially CPET, combined with imaging modalities like stress echocardiography or stress magnetic resonance imaging (MRI) provides valuable information on exercise tolerance, RV function under stress, and inducible ischemia. These parameters help in identifying patients at higher risk of adverse outcomes and guide the timing of interventions such as PVR (27,37).

Clinical implications

The integration of these imaging modalities into a comprehensive follow-up protocol allows for early detection of complications, timely intervention, and improved long-term outcomes in rTOF. Risk stratification based on imaging findings helps in:

(I) Timing of PVR: indications for PVR include severe PR, RV dilation, and dysfunction. Imaging parameters such as right ventricular enddiastolic volume index (RVEDVI) >160 mL/m^2, indexed RV end-systolic volume >80 mL/m^2, or

(II) RV-LV end-diastolic volume ratio >2.0, are crucial in decision-making (16);

(III) Monitoring RV function: regular assessment of RV size, mass and function is essential for predicting and preventing RV failure as well as monitoring LV systolic function and strain (26,59);

(IV) Detection of arrhythmias: identifying patients at risk for arrhythmias through imaging and ECG parameters allows for early intervention with antiarrhythmic therapy or ICDs.

Conclusions

CMR has emerged as an important and valuable non-invasive and non-ionizing tool in assessing TOF preoperatively in pediatrics, but especially in monitoring the development of postoperative complications early and later in life. CMR with traditional sequences using criteria as PR and increased RV volume and decreased function are helpful in the decision making to find the optimal timepoint for reintervention. However, these criteria are still under debate and novel CMR techniques, such as 4D flow, tissue characterization and strain carry more advanced and refined hemodynamic and functional information for risk stratification. These new methods reveal promising in gaining more importance in the evaluation of patients with rTOF.

Acknowledgments

None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Harald Kaemmerer) for the series "Current Management Aspects of Adult Congenital Heart Disease (ACHD): Part VI" published in *Cardiovascular Diagnosis and Therapy*. The article has undergone external peer review.

Peer Review File: Available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-378/prf

Funding: None.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-378/coif). The series "Current Management Aspects of Adult Congenital Heart Disease (ACHD): Part VI" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Valente AM, Cook S, Festa P, et al. Multimodality imaging guidelines for patients with repaired tetralogy of fallot: a report from the AmericanSsociety of Echocardiography: developed in collaboration with the Society for Cardiovascular Magnetic Resonance and the Society for Pediatric Radiology. J Am Soc Echocardiogr 2014;27:111-41.
2. Fogel MA, Anwar S, Broberg C, et al. Society for Cardiovascular Magnetic Resonance/European Society of Cardiovascular Imaging/American Society of Echocardiography/Society for Pediatric Radiology/North American Society for Cardiovascular Imaging Guidelines for the use of cardiovascular magnetic resonance in pediatric congenital and acquired heart disease : Endorsed by The American Heart Association. J Cardiovasc Magn Reson 2022;24:37.
3. Chiu SN, Wang JK, Chen HC, et al. Long-term survival and unnatural deaths of patients with repaired tetralogy of Fallot in an Asian cohort. Circ Cardiovasc Qual Outcomes 2012;5:120-5.
4. Persson J, Gyllencreutz Castellheim A, Dellborg M, et al. Survival Trends in Children With Tetralogy of Fallot in Sweden From 1970 to 2017. JAMA Netw Open 2023;6:e2314504.
5. Bové T. Surgical repair of tetralogy of Fallot: the quest for the 'ideal' repair. Transl Pediatr 2017;6:64-6.
6. Al Mosa A, Bernier PL, Tchervenkov CI. Considerations in Timing of Surgical Repair in Tetralogy of Fallot. CJC Pediatr Congenit Heart Dis 2023;2:361-7.
7. Goldstein BH, Petit CJ, Qureshi AM, et al. Comparison of Management Strategies for Neonates With Symptomatic Tetralogy of Fallot. J Am Coll Cardiol 2021;77:1093-106.
8. Bailey J, Elci OU, Mascio CE, et al. Staged Versus Complete Repair in the Symptomatic Neonate With Tetralogy of Fallot. Ann Thorac Surg 2020;109:802-8.
9. Ramakrishnan KV, Zurakowski D, Pastor W, et al. Symptomatic Tetralogy of Fallot in Young Infants: Primary Repair or Shunt-Pediatric Health Information System Database Analysis. World J Pediatr Congenit Heart Surg 2018;9:539-45.
10. Qureshi AM, Caldarone CA, Wilder TJ. Transcatheter Approaches to Palliation for Tetralogy of Fallot. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2022;25:48-57.
11. Vanderlaan RD, Barron DJ. Optimal Surgical Management of Tetralogy of Fallot. CJC Pediatr Congenit Heart Dis 2023;2:352-60.
12. Blais S, Marelli A, Vanasse A, et al. Comparison of Long-term Outcomes of Valve-Sparing and Transannular Patch Procedures for Correction of Tetralogy of Fallot. JAMA Netw Open 2021;4:e2118141.
13. Schulte LJ, Miller PC, Bhat AN, et al. Evolution of Pulmonary Valve Management During Repair of Tetralogy of Fallot: A 14-year Experience. Ann Thorac Surg 2023;115:462-9.
14. Expert Consensus Panel; Miller JR, Stephens EH, et al. The American Association for Thoracic Surgery (AATS) 2022 Expert Consensus Document: Management of infants and neonates with tetralogy of Fallot. J Thorac Cardiovasc Surg 2023;165:221-50.
15. Gatzoulis MA, Balaji S, Webber SA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. Lancet 2000;356:975-81.
16. Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;139:e698-800.
17. Geva T. Indications for pulmonary valve replacement in repaired tetralogy of fallot: the quest continues. Circulation 2013;128:1855-7.
18. Leonardi B, Perrone M, Calcaterra G, et al. Repaired Tetralogy of Fallot: Have We Understood the Right Timing of PVR? J Clin Med 2024;13:2682.
19. Bokma JP, Geva T, Sleeper LA, et al. Improved Outcomes After Pulmonary Valve Replacement in Repaired Tetralogy of Fallot. J Am Coll Cardiol 2023;81:2075-85.
20. Baumgartner H, De Backer J, Babu-Narayan SV, et al. 2020 ESC Guidelines for the management of adult congenital heart disease. Eur Heart J 2021;42:563-645.
21. van der Ven JPG, van den Bosch E, Bogers AJCC, et al. Current outcomes and treatment of tetralogy of Fallot. F1000Res 2019;8:F1000 Faculty Rev-1530.
22. Snygg-Martin U, Giang KW, Dellborg M, et al. Cumulative Incidence of Infective Endocarditis in Patients

with Congenital Heart Disease: A Nationwide, Case-Control Study Over Nine Decades. Clin Infect Dis 2021;73:1469-75.
23. Delgado V, Ajmone Marsan N, de Waha S, et al. 2023 ESC Guidelines for the management of endocarditis. Eur Heart J 2023;44:3948-4042.
24. Ishigami S, Ye XT, Buratto E, et al. Long-term outcomes of tetralogy of Fallot repair: A 30-year experience with 960 patients. J Thorac Cardiovasc Surg 2024;167:289-302.e11.
25. Dennis M, Moore B, Kotchetkova I, et al. Adults with repaired tetralogy: low mortality but high morbidity up to middle age. Open Heart 2017;4:e000564.
26. Apostolopoulou SC, Manginas A, Kelekis NL, et al. Cardiovascular imaging approach in pre and postoperative tetralogy of Fallot. BMC Cardiovasc Disord 2019;19:7.
27. Moscatelli S, Pergola V, Motta R, et al. Multimodality Imaging Assessment of Tetralogy of Fallot: From Diagnosis to Long-Term Follow-Up. Children (Basel) 2023;10:1747.
28. Kino A, Zucker EJ, Honkanen A, et al. Ultrafast pediatric chest computed tomography: comparison of free-breathing vs. breath-hold imaging with and without anesthesia in young children. Pediatr Radiol 2019;49:301-7.
29. Dirrichs T, Tietz E, Rüffer A, et al. Photon-counting versus Dual-Source CT of Congenital Heart Defects in Neonates and Infants: Initial Experience. Radiology 2023;307:e223088.
30. Mandalenakis Z, Karazisi C, Skoglund K, et al. Risk of Cancer Among Children and Young Adults With Congenital Heart Disease Compared With Healthy Controls. JAMA Netw Open 2019;2:e196762.
31. Caris E, Drant S. Assessment of regional and global right ventricular systolic function in children with repaired tetralogy of Fallot. Cardiol Young 2021;31:1571-5.
32. Johansson B, Babu-Narayan SV, Kilner PJ. The effects of breath-holding on pulmonary regurgitation measured by cardiovascular magnetic resonance velocity mapping. J Cardiovasc Magn Reson 2009;11:1.
33. Elsayed A, Gilbert K, Scadeng M, et al. Four-dimensional flow cardiovascular magnetic resonance in tetralogy of Fallot: a systematic review. J Cardiovasc Magn Reson 2021;23:59.
34. Soulat G, Alattar Y, Ladouceur M, et al. Discordance between 2D and 4D flow in the assessment of pulmonary regurgitation severity: a right ventricular remodeling follow-up study. Eur Radiol 2023;33:5455-64.
35. Cruz C, Pinho T, Madureira AJ, et al. Is it important to assess the ascending aorta after tetralogy of Fallot repair? Rev Port Cardiol (Engl Ed) 2018;37:773-9.
36. Tirilomis T, Friedrich M, Zenker D, et al. Indications for reoperation late after correction of tetralogy of Fallot. Cardiol Young 2010;20:396-401.
37. Ghonim S, Gatzoulis MA, Ernst S, et al. Predicting Survival in Repaired Tetralogy of Fallot: A Lesion-Specific and Personalized Approach. JACC Cardiovasc Imaging 2022;15:257-68.
38. Babu-Narayan SV, Kilner PJ, Li W, et al. Ventricular fibrosis suggested by cardiovascular magnetic resonance in adults with repaired tetralogy of fallot and its relationship to adverse markers of clinical outcome. Circulation 2006;113:405-13.
39. Harrington SG, Jaimes C, Weagle KM, et al. Strategies to perform magnetic resonance imaging in infants and young children without sedation. Pediatr Radiol 2022;52:374-81.
40. Zaki N, Parra D, Wells Q, et al. Assessment of gadolinium deposition in the brain tissue of pediatric and adult congenital heart disease patients after contrast enhanced cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2020;22:82.
41. Endrikat J, Gutberlet M, Hoffmann KT, et al. Clinical Safety of Gadobutrol: Review of Over 25 Years of Use Exceeding 100 Million Administrations. Invest Radiol 2024;59:605-13.
42. Casto T, Kollar S, Sawda C, et al. Hemodynamic Assessment of Infants With Congenital Heart Disease Using Ferumoxytol-Enhanced 4D Flow Cardiac Magnetic Resonance. JACC Case Rep 2024;29:102559.
43. Koechli M, Callaghan FM, Burkhardt BEU, et al. Accelerated cardiac magnetic resonance imaging using deep learning for volumetric assessment in children. Pediatr Radiol 2024;54:1674-85.
44. Gatehouse PD, Keegan J, Crowe LA, et al. Applications of phase-contrast flow and velocity imaging in cardiovascular MRI. Eur Radiol 2005;15:2172-84.
45. Lagerstrand K, Nyström A, Svensson PA, et al. Accurate quantification of pulmonary perfusion ratio in children with congenital heart disease using partial volume corrected 4D flow cardiac magnetic resonance. Front Pediatr 2024;12:1339679.
46. De Leon-Benedetti LS, Ramirez-Suarez KI, Otero HJ, et al. How we do it: Cardiac implantable devices are not a contraindication to MRI: time for a paradigm shift. Pediatr Radiol 2024;54:863-75.
47. Gakenheimer-Smith L, Etheridge SP, Niu MC, et al. MRI

in pediatric and congenital heart disease patients with CIEDs and epicardial or abandoned leads. Pacing Clin Electrophysiol 2020;43:797-804.
48. Zucker EJ. Compact pediatric cardiac magnetic resonance imaging protocols. Pediatr Radiol 2023;53:1336-51.
49. Copeland A, Silver E, Korja R, et al. Infant and Child MRI: A Review of Scanning Procedures. Front Neurosci 2021;15:666020.
50. Janos S, Schooler GR, Ngo JS, et al. Free-breathing unsedated MRI in children: Justification and techniques. J Magn Reson Imaging 2019;50:365-76.
51. Hundley WG, Bluemke DA, Bogaert J, et al. Society for Cardiovascular Magnetic Resonance (SCMR) guidelines for reporting cardiovascular magnetic resonance examinations. J Cardiovasc Magn Reson 2022;24:29.
52. Dorfman AL, Geva T, Samyn MM, et al. SCMR expert consensus statement for cardiovascular magnetic resonance of acquired and non-structural pediatric heart disease. J Cardiovasc Magn Reson 2022;24:44.
53. Voges I, Raimondi F, McMahon CJ, et al. Clinical impact of novel cardiovascular magnetic resonance technology on patients with congenital heart disease: a scientific statement of the Association for European Pediatric and Congenital Cardiology and the European Association of Cardiovascular Imaging of the European Society of Cardiology. Eur Heart J Cardiovasc Imaging 2024;25:e274-e294. Erratum in: Eur Heart J Cardiovasc Imaging 2024;25:e295.
54. Bissell MM, Raimondi F, Ait Ali L, et al. 4D Flow cardiovascular magnetic resonance consensus statement: 2023 update. J Cardiovasc Magn Reson 2023;25:40.
55. Singh AAV, Yoo SJ, Seed M, et al. Recent advances in multimodal imaging in tetralogy of fallot and double outlet right ventricle. Curr Opin Cardiol 2024;39:323-30.
56. Aquino GJ, Mastrodicasa D, Alabed S, et al. Radiology: Cardiothoracic Imaging Highlights 2023. Radiol Cardiothorac Imaging 2024;6:e240020.
57. Dyverfeldt P, Bissell M, Barker AJ, et al. 4D flow cardiovascular magnetic resonance consensus statement. J Cardiovasc Magn Reson 2015;17:72.
58. Warmerdam EG, Neijzen RL, Voskuil M, et al. Four-dimensional flow CMR in tetralogy of fallot: current perspectives. Br J Radiol 2022;95:20210298.
59. Ghonim S, Babu-Narayan SV. Use of Cardiovascular Magnetic Resonance for Risk Stratification in Repaired Tetralogy of Fallot. CJC Pediatr Congenit Heart Dis 2023;2:393-403.
60. Hsiao A, Lustig M, Alley MT, et al. Rapid pediatric cardiac assessment of flow and ventricular volume with compressed sensing parallel imaging volumetric cine phase-contrast MRI. AJR Am J Roentgenol 2012;198:W250-9.
61. Hsiao A, Alley MT, Massaband P, et al. Improved cardiovascular flow quantification with time-resolved volumetric phase-contrast MRI. Pediatr Radiol 2011;41:711-20.
62. Gabbour M, Schnell S, Jarvis K, et al. 4-D flow magnetic resonance imaging: blood flow quantification compared to 2-D phase-contrast magnetic resonance imaging and Doppler echocardiography. Pediatr Radiol 2015;45:804-13.
63. Riesenkampff E, Luining W, Seed M, et al. Increased left ventricular myocardial extracellular volume is associated with longer cardiopulmonary bypass times, biventricular enlargement and reduced exercise tolerance in children after repair of Tetralogy of Fallot. J Cardiovasc Magn Reson 2016;18:75.
64. Yim D, Riesenkampff E, Caro-Dominguez P, et al. Assessment of Diffuse Ventricular Myocardial Fibrosis Using Native T1 in Children With Repaired Tetralogy of Fallot. Circ Cardiovasc Imaging 2017;10:e005695.
65. Cochet H, Iriart X, Allain-Nicolaï A, et al. Focal scar and diffuse myocardial fibrosis are independent imaging markers in repaired tetralogy of Fallot. Eur Heart J Cardiovasc Imaging 2019;20:990-1003.
66. Ghonim S, Ernst S, Keegan J, et al. Three-Dimensional Late Gadolinium Enhancement Cardiovascular Magnetic Resonance Predicts Inducibility of Ventricular Tachycardia in Adults With Repaired Tetralogy of Fallot. Circ Arrhythm Electrophysiol 2020;13:e008321.
67. Kapel GF, Sacher F, Dekkers OM, et al. Arrhythmogenic anatomical isthmuses identified by electroanatomical mapping are the substrate for ventricular tachycardia in repaired Tetralogy of Fallot. Eur Heart J 2017;38:268-76.
68. Suther KR, Hopp E, Geier O, et al. Diffuse myocardial fibrosis in adolescents operated with arterial switch for transposition of the great arteries - A CMR study. Int J Cardiol 2019;276:100-6.
69. de Lange C, Quattrone A, Try K, et al. Is experienced pregnancy in women with repaired tetralogy of Fallot related to diffuse myocardial fibrosis? Int J Cardiol 2021;344:95-102.
70. Messroghli DR, Moon JC, Ferreira VM, et al. Clinical recommendations for cardiovascular magnetic resonance

mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI). J Cardiovasc Magn Reson 2017;19:75.
71. Kellman P, Hansen MS. T1-mapping in the heart: accuracy and precision. J Cardiovasc Magn Reson 2014;16:2.
72. Chen CA, Dusenbery SM, Valente AM, et al. Myocardial ECV Fraction Assessed by CMR Is Associated With Type of Hemodynamic Load and Arrhythmia in Repaired Tetralogy of Fallot. JACC Cardiovasc Imaging 2016;9:1-10.
73. O'Brien AT, Gil KE, Varghese J, et al. T2 mapping in myocardial disease: a comprehensive review. J Cardiovasc Magn Reson 2022;24:33.
74. Burris NS, Lima APS, Hope MD, et al. Feature Tracking Cardiac MRI Reveals Abnormalities in Ventricular Function in Patients With Bicuspid Aortic Valve and Preserved Ejection Fraction. Tomography 2018;4:26-32.
75. Thomas SK, DSouza R, Hanneman K, et al. Prognostic value of myocardial deformation parameters for outcome prediction in tetralogy of Fallot. J Cardiovasc Magn Reson 2024;26:101054.
76. Rajiah PS, Kalisz K, Broncano J, et al. Myocardial Strain Evaluation with Cardiovascular MRI: Physics, Principles, and Clinical Applications. Radiographics 2022;42:968-90.
77. André F, Robbers-Visser D, Helling-Bakki A, et al. Quantification of myocardial deformation in children by cardiovascular magnetic resonance feature tracking: determination of reference values for left ventricular strain and strain rate. J Cardiovasc Magn Reson 2016;19:8.
78. Shang Q, Patel S, Steinmetz M, et al. Myocardial deformation assessed by longitudinal strain: Chamber specific normative data for CMR-feature tracking from the German competence network for congenital heart defects. Eur Radiol 2018;28:1257-66.
79. Voges I, Negwer I, Caliebe A, et al. Myocardial Deformation in the Pediatric Age Group: Normal Values for Strain and Strain Rate Using 2D Magnetic Resonance Feature Tracking. J Magn Reson Imaging 2022;56:1382-92.
80. Doan TT, Molossi S, Sachdeva S, et al. Dobutamine stress cardiac MRI is safe and feasible in pediatric patients with anomalous aortic origin of a coronary artery (AAOCA). Int J Cardiol 2021;334:42-8.
81. Parish V, Valverde I, Kutty S, et al. Higher dose dobutamine stress MR imaging in repaired Tetralogy of Fallot: observer variance of volumetric assessment compared with normal volunteers. J Magn Reson Imaging 2013;38:1356-61.
82. Moura Cunha G, Fan B, Navin PJ, et al. Interpretation, Reporting, and Clinical Applications of Liver MR Elastography. Radiology 2024;310:e231220.
83. Caenen A, Bézy S, Pernot M, et al. Ultrasound Shear Wave Elastography in Cardiology. JACC Cardiovasc Imaging 2024;17:314-29.
84. Mazumder R, Schroeder S, Mo X, et al. In vivo quantification of myocardial stiffness in hypertensive porcine hearts using MR elastography. J Magn Reson Imaging 2017;45:813-20.
85. Arani A, Murphy MC, Bhopalwala H, et al. Sex Differences in Aging-related Myocardial Stiffening Quantitatively Measured with MR Elastography. Radiol Cardiothorac Imaging 2024;6:e230140.
86. Nielles-Vallespin S, Khalique Z, Ferreira PF, et al. Assessment of Myocardial Microstructural Dynamics by In Vivo Diffusion Tensor Cardiac Magnetic Resonance. J Am Coll Cardiol 2017;69:661-76.
87. Valente AM, Gauvreau K, Assenza GE, et al. Contemporary predictors of death and sustained ventricular tachycardia in patients with repaired tetralogy of Fallot enrolled in the INDICATOR cohort. Heart 2014;100:247-53.
88. Majeed A, Geva T, Sleeper LA, et al. Cardiac MRI predictors of good long-term outcomes in patients with repaired TOF. Am Heart J 2022;245:70-7.
89. Avesani M, Borrelli N, Krupickova S, et al. Echocardiography and cardiac magnetic resonance in children with repaired tetralogy of Fallot: New insights in cardiac mechanics and exercise capacity. Int J Cardiol 2020;321:144-9.
90. van Grootel RWJ, van den Bosch AE, Baggen VJM, et al. The Prognostic Value of Myocardial Deformation in Adult Patients With Corrected Tetralogy of Fallot. J Am Soc Echocardiogr 2019;32:866-875.e2.
91. Egbe AC, Miranda WR, Madhavan M, et al. Right atrial dysfunction is associated with atrial arrhythmias in adults with repaired tetralogy of fallot. Am Heart J 2023;263:141-50.
92. Bonello B, Kempny A, Uebing A, et al. Right atrial area and right ventricular outflow tract akinetic length predict sustained tachyarrhythmia in repaired tetralogy of Fallot.

Int J Cardiol 2013;168:3280-6.
93. Hanneman K, Crean AM, Wintersperger BJ, et al. The relationship between cardiovascular magnetic resonance imaging measurement of extracellular volume fraction and clinical outcomes in adults with repaired tetralogy of Fallot. Eur Heart J Cardiovasc Imaging 2018;19:777-84.

Cite this article as: Nyström A, Berntsson C, Mandalenakis Z, Lagerstrand K, Dangardt F, de Lange C. Cardiovascular magnetic resonance in Tetralogy of Fallot—state of the art. Cardiovasc Diagn Ther 2025;15(1):173-194. doi: 10.21037/cdt-24-378